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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,902	01/09/2006	Roland Schule	033-004	5822

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CERMAK NAKAJIMA LLP
127 S. Peyton Street, Suite 210
ALEXANDRIA, VA 22314

EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	**PAPER NUMBER**
1633	

NOTIFICATION DATE	DELIVERY MODE
07/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

CGOODE@CermakNakajima.COM
IP@CermakNakajima.com
ACERMAK@CermakNakajima.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,902	SCHULE ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 04/26/2010 in response to office action mailed on 11/27/2009 has been acknowledged.

Claims 1 is amended.

Claim 20 is canceled.

Claims 1-6 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Examiner's comments

Withdrawn: Claims *1-6 and 20* are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. for the reason of record as set forth in the office action mailed on 11/27/2009 is withdrawn in view Applicants amendments to claims.

Withdrawn: Claims 1-6 and 20 are rejected under 35 USC 103 (a) as being unpatentable over Lai et al (2002, J. Bone and Mineral Res. Vol.17; supp (1), pp. S129; art of record) in view of Marie et al (2002, Histol. Histopathol. 17:877-885), Amaar et al (2002, J. Biol. Chem. 277:12503-12059; art of record) and Muller et al (2002, The EMBO Journal 21:736-748; art of record). for the reason of record as set forth in the office action mailed on 11/27/2009 is withdrawn in view Applicants amendments to claims and in view of revised 35USC103 rejections below.

Withdrawn: Claims 1-6 and 20 are rejected under 35 U.S.C. 112, first paragraph, over the scope of enablement of the specification, for the reason of record as set forth in the office action mailed on 11/27/2009 is withdrawn in view Applicants amendments to claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim. Method steps of the claim require identifying a compound that increases FHL2 activity in an osteoblast by testing said compound both in vitro and in vivo. However the claim concludes testing either in vitro or in vivo is enough to achieve the same, and there is no clear indication of what activity is being tested such that it would necessarily work in the claimed method. The Applicant should consider appropriately amending the claim.

Claims 2-6 are rejected for depending from a rejected base claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 are rejected under 35 USC 103 (a) as being unpatentable over Lai et al (2002, J. Bone and Mineral Res. Vol.17; supp (1), pp. S129; art of record), Amaar et al (2002, J. Biol. Chem. 277:12503-12059; art of record) and Muller et al (2002, The EMBO Journal 21:736-748; art of record).

The above claims are drawn to a method of identifying a test compound that increases FHL2 expression or activity in an osteoblast comprising the steps contacting at least one osteoblast in vitro with a test compound and determining the FHL2 protein level, comparing the same with FHL2 protein level in a control osteoblast cell,

determining whether the test compound is capable of an action selected from a Markush group of actions including i) increasing FHL2 expression or activity in a osteoblast in vivo, ii) increasing Fhl2/RunX interaction in osteoblasts in vivo and iii) promoting the formation of ECM in a non-human test animal or iv) a combination thereof and determining either based on said in vitro steps or said in vivo steps for selecting the test compound as compound that increases Fhl2 expression or activity. In further limitations different ways of estimating Fhl2 protein in an osteoblast, use of different osteoblast cell lines and preparing the compound for treating a bone disease..

Regarding the claims 1-6 Lai teaches that over expressing FHL2 gene and protein in osteoblasts (MC3T3-E1) in vitro by contacting FHL2 cDNA (a compound) cloned in an expression vector (Abstract). Lai further teaches Fhl2 expression is up regulated in these cells which further show an increase in cell proliferation, matrix mineralization, osteocalcin up regulation and Runx2 (Cbfa1) up regulation. Lai further teaches that FHL2 may play an important role in bone formation in vitro and in vivo. Lai clearly teaches FHL2 up-regulates osteoblast growth and differentiation and potentiates FGF2 activity that plays an important role in osteoblast activity and bone formation in vivo. Lai however, does not teach or contemplate determining the level of interaction between Fhl2 protein and Runx2 protein in the osteoblast.

Regarding the claims Amaar teaches over expressing FHL2 gene and protein in bone cells (U2 osteoblasts or osteosarcoma cells) in vitro by contacting FHL2 cDNA (a compound) cloned in retroviral expression vector (p.12054, col.2, paragraph 8 bridging p.1205; p.12059, col.1, paragraphs 3-5 bridging col.2). Amaar further teaches that Fhl2 is strongly localized in the nucleus and interacts with IGBF5, an mportant bone formation regulator (abstract; p.12059, col.1, paragraphs 3-5 bridging col.2). Besides this FHL2 has been shown to interact with other proteins involved in transcription regulation in osteoblasts and the presence of multiple lim domains and zinc finger motifs may facilitate these interactions (p.12059, col.1, paragraphs 3-5 bridging col.2).

Muller teaches that Fhl2 is transcriptional co-activator and that FHL2 binds and selectively activates the transcriptional activity of androgen receptors (entire article; Abstract; p.746, col.2, 2nd paragraph). Muller further clearly teaches synthetic

compounds cellular compounds capable of activating signaling pathway that stimulates FHL2 expression in cells (p.739; p.742 col. 1 bridging col.2).

Thus it would have been obvious to one of skill in the art to identify compounds that increase FHL2 expression or activity in an osteoblast at least in vitro condition as taught by Lai and further establish the at least some of these compounds (for e.g., cDNA expression) can increase Fhl2 expression in an osteoblast in vivo. One of skill in the art would have been motivated to increase the level of Fhl2 expression or activity in a osteoblast in order increase its proliferation or bone forming activity. One of skill in the art would have expectation of success as the art teaches that it is routine to express a gene in a cell in vitro or in vivo Thus the invention was prima facie obvious to the Artisan at the time of invention.

Conclusion

No claim allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday

through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.,* may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633